This report contains the collective views of an international group of experts and does not necessarily represent the decision or the stated policy of the World Health Organization.

WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES
No. 230

CALCIUM REQUIREMENTS

Report of an FAO/WHO Expert Group

Rome, Italy, 23 to 30 May 1961

Published jointly by FAO and WHO
and also issued as
FAO Nutrition Meetings Report
Series No. 30

WORLD HEALTH ORGANIZATION
GENEVA
1962

Printed in Italy

CONTENTS

INTRODUCTION

Nutritional improvement is an important objective of the Food and Agriculture Organization of the United Nations (FAO) and of the World Health Organization (WHO) and efforts to raise levels of nutrition throughout the world have been prominent in the programs of both organizations. Success in such efforts, however, can be judged only in the light of an adequate knowledge of the nutritional requirements of different populations living and working under widely varying conditions. In the absence of appropriate dietary standards it is impossible either to orient programs toward better nutrition, in the fields both of food and agriculture and of public health, or to evaluate their effectiveness. The subject of nutritional requirements has therefore received the continuous attention of FAO and WHO for many years and considerable progress has already been made with respect to calories and proteins with the assistance of the respective committees convened by FAO on these two aspects (14, 15).

Next to the problem of establishing requirements for calories and proteins, it was thought that the question of calcium requirement deserved early attention, particularly because of considerable uncertainty and conflicting views on this matter. On the one hand, more people fail to get the currently recommended allowances of calcium than of any other nutrient, while on the other hand, it is recognized that there is little convincing evidence of specific disabilities attributable to dietary calcium deficiency. This situation might not be of urgent concern but for its implications in large-scale programs designed to achieve nutritional improvement. In many parts of the world, especially in the developing regions, only limited opportunities exist for the quick or inexpensive intake of calcium, conforming to standards in current use, through the consumption of ordinary foods. This has naturally led to suggestions for the widespread fortification of foods with calcium. Such large-scale programs,

however, can be expensive and difficult to achieve technically and to organize efficiently, even with relatively cheap sources of this nutrient. Besides, in the long run, nutritional improvements ought to be achieved through a better basic diet and not by supplementation with individual nutrients. These facts point clearly to the importance of reaching reliable conclusions on the calcium needs of different population groups.

The Group was aware that the inadequacy of present knowledge did not permit unequivocal answers to many questions posed in this connection, nor was it possible to specify the amounts of calcium required under different physiological and environmental conditions. Nevertheless, a review of current knowledge was considered useful so as to expose the crucial gaps in factual information, indicate possible means of filling these gaps and, finally, to suggest tentative allowances of calcium to be used in practical programs pending consideration of the problem at a later date when the results of further research would be available.

1. METHOD OF APPROACH

A historical review of the literature dealing with calcium metabolism and calcium requirements was obviously beyond the scope of this report. The Group approached its task with the help of specially prepared working papers which summarized the information available on relevant aspects. A number of recent reviews (19, 33, 36, 40, 45, 50) dealing with calcium requirements and associated fields greatly facilitated the preparation of these papers. The present report represents the consensus of opinion arrived at after consideration and discussion of the material in the working papers. No attempt has therefore been made to provide complete documentation of all the literature forming the basis of the conclusions drawn, although some of the pertinent papers are cited. Such a procedure inevitably does injustice to many workers in many countries who have contributed to the research in this field. Thus, the familiar device of referring to review papers has often been used both to take advantage of the contributions provided by such reviews and to avoid the often difficult task of selecting one or two papers from a number which may be equally meritorious.

In 1936, the Technical Commission of the Health Committee, League of Nations (62) made recommendations for quantitative calorie and protein requirements and the consumption of appropriate "protective foods" was urged to provide minerals and vitamins. No attempt was made, however, to establish requirements or recommendations for specific minerals or vitamins. Since that time many national groups have produced tables of nutritional requirements, allowances, or standards which include numerical values for calcium. Some of these are well known and have been widely used.

In general, the standards for adults have been based largely upon estimates of the amount of calcium required to maintain calcium balance. Similar data for children and for pregnant and lactating women are also available and these have been supplemented or modified by calculations

of the amount of calcium which may be required for the formation of the skeleton or for the secretion of milk. Such calculations require several assumptions to be made. As a result, large differences in the calcium balance data available and in calculated values (depending upon the assumptions made) have led to divergent opinions as to their significance. Most of the experimental data have been obtained in countries where calcium consumption is relatively high and little attention has usually been paid to the habitual calcium intake of the subjects studied. For the most part also, the studies have been of rather short duration and have often yielded calcium retentions which are impossibly high when projected over long periods of time.

ADAPTATION

In this report, reference is made repeatedly to "adaptation." In a general sense this describes the ability of man and other animals to live and develop in widely divergent environmental conditions, including great differences in diet composition. It should be noted that adaptation to diet is a necessary condition for survival in any circumstances and the term applies equally well to high, low or moderate intakes, or to diets in which the availability of essential nutrients may initially be low. Thus, adaptation *per se* carries no connotation of an undesirable process. It is only in those circumstances in which the intake of a nutrient is so high or so low as to exceed the capacity of the body to adapt completely that ill-health will result.

Adaptation is also applied in a somewhat more restricted sense with regard to calcium. As the intake of calcium is lowered, the efficiency of the body to absorb and retain calcium increases, while raising the intake may result in reduced utilization. This ability to adapt may be measured by appropriately designed calcium balance studies. However, it will be apparent that such studies, of rather short duration compared to the lifetime of man, do not indicate complete adaptation in the broad sense that optimal health may be achieved at all levels of intake at which calcium balance is reached.

2. SURVEY OF INTAKES AND DIETARY SOURCES OF CALCIUM

Data on patterns and levels of food consumption may be derived from food balance sheets and from dietary surveys among representative groups of households and individuals. Consumption data from food balance sheets relate to national or territorial populations as a whole (17). They are derived by adjusting the quantities of foods produced with corrections for imports and exports, for changes in stocks and for amounts which for other reasons become unavailable for direct human consumption. These derived figures, divided by the number of the population, represent the *per caput* supplies available for human consumption at the "retail level," that is, foods leaving the retail store in the shopping basket or reaching the kitchen before preparation for cooking.

For information on the *per caput* consumption of different foods and nutrients by different sections of the population, for example, by regions, economic or social levels, age, sex and occupation, it is necessary to investigate directly the amounts of various foods consumed by households or persons in those sections of the population.

Information from food balance sheets is particularly unsatisfactory as regards assessment of the calcium intake, since statistical data on the availability of some of the main sources of calcium, viz., dairy products, fish and vegetables, are often extremely limited. Furthermore, the breakdown of different groups of foodstuffs into specific foods is often not sufficiently detailed to enable the calcium content to be calculated with any reasonable degree of assurance. For instance, the difference between the calcium content of deep-green leafy vegetables and that of other vegetables and between that of small fish (eaten whole with bones) and bigger fish is important, but available statistics do not usually differentiate between them. Nor do estimates based on food balance sheets generally take into account the effects of food processing and preparation, such as the addition of calcium carbonate (*creta praeparata*) to flour, as in the

United Kingdom, or of lime in the making of maize tortillas in Mexico and Central America (7).

Nevertheless, national food balance sheets can serve to give a broad estimate of the calcium contributed by the major food groups. Recent available data for a period of one year from 17 selected countries are shown in Appendix 1. From these values it is clear not only that the total calcium supply varies widely from country to country, but also that variation exists in the relative contribution of different food groups to the calcium supply. The countries shown can be grouped into four broad categories: the *first* includes most of Europe, North America and Oceania, with as much as 900 mg or more of calcium *per caput* per day, of which 70 to 90 percent is obtained from milk and its products; the *second* includes some southern European countries, such as Italy, and some Latin American countries, such as Argentina, with 650 to 800 mg a day, of which about 50 to 70 percent comes from milk and milk products but to which vegetables tend to make a relatively more important contribution than in the first category; the *third* includes Chile, India, South Africa, Turkey and the United Arab Republic, with a much smaller total calcium supply of about 350 to 500 mg *per caput* daily, of which the proportion from milk and its products is important (30 to 65 percent), but cereals, pulses, nuts and vegetables also make significant contributions; and the *fourth* includes countries like Japan, where the daily supply of some 350 mg or less is derived fairly evenly from cereals, pulses, nuts and vegetables, but to which milk does not make a major contribution. Only in a few countries, such as Chile and Japan, does fish appear to make any significant contribution to the calcium supply.

Similar indications of quantities and sources of calcium can be gained from the results of family food consumption surveys, some of which are given in Appendix 2. Calcium intakes differ considerably, not only from one country to another, but also between different sections of the population within the same country. Persons in the upper economic levels generally have a higher calcium intake and, within each economic level, rural populations seem to have a higher intake than those in urban areas, although such differences tend to lessen as countries develop economically and industrially. In any country there are wide variations from family to family, and between males and females, especially beyond early childhood. In the United States, for example, intake of calcium by teen-age girls and women tends to be considerably lower than that of men and boys, reflecting in part a lower total food intake after 12 years of age, and in part a lower consumption of milk (Appendix 3).

Unusual food habits or food processing and preparation practices which exist in different parts of the world may make unexpected contributions to the dietary intake of calcium. In some places, drinking water or water used in beverages and food preparation may contribute measurably to calcium intake. Also, there are items of diet in certain countries that are exceptionally rich in calcium, such as ragi (*Eleusine coracana*), quinoa (*Chenopodium quinoa*) and related species, and sesame seed (*Sesamum indicum*). The chewing of betel leaves with lime may also add considerably to calcium intake. Conversely, calcium may be lost to varying extents during food processing and household preparation before consumption, as by the milling of grains, discarding parts of vegetables before cooking, or the boiling of foods in large amounts of water low in calcium.

Clearly, a reliable appraisal of calcium in diets requires accurate information both on food consumption, preferably obtained by means of direct consumption surveys, and on the calcium content of the foods consumed.

3. REVIEW OF EVIDENCE OF ILL-HEALTH POSSIBLY RELATED TO LOW OR HIGH INTAKES OF CALCIUM

Most apparently healthy people — children and adults — throughout the world develop and live satisfactorily on a dietary intake of calcium which lies between 300 mg and over 1,000 mg a day. There is so far no convincing evidence that, in the absence of nutritional disorders and especially when the vitamin D status is adequate, an intake of calcium even below about 300 mg or above 1,000 mg a day is harmful. Nevertheless, theoretical considerations indicate that a calcium intake much below 300 mg a day is certain to be harmful.

When a diet is very low in one or more of the essential nutrients, such as proteins and some vitamins and mineral salts, the nature of the stigmata is predictable. These stigmata will generally be remediable by treatment with the relevant nutrients. This should also apply to calcium, but the clinical and pathological stigmata in man are not known with certainty, even under conditions of very low intake (below 300 mg per day). The best approach to the investigation of the problem of calcium deficiency, therefore, seems to be to study the integrity of physiological processes involving calcium under conditions of low calcium intake and the effect of the addition of calcium salts.

Effects on the skeleton

Period of growth

1. While growth in children is relatively slow in populations in developing regions, it is questionable whether slower growth in otherwise healthy children is necessarily deleterious. To what extent retarded growth is due specifically to a low calcium intake is not known. Studies of Central American populations with increased calcium intake from lime-treated tortillas (7), and of certain South African Bantu groups

consuming highly saline drinking water, suggest that the level of calcium intake may not be critical. Aykroyd and Krishnan (2) found, however, that calcium lactate supplements stimulated growth in poor Indian children over a period of months. It must be kept in mind that good growth is a useful criterion of the adequacy of a certain nutrient *only* when all other factors (dietary and nondietary) are adequately controlled. Obviously, such control is virtually impossible when comparing different population groups, such as Americans, Europeans, Bantu and Indians, because of differences in race, diet, manner of life and environmental conditions. Further information on these aspects is urgently needed. However, on theoretical grounds, taking into account the daily accretions of calcium required for growth, the Group believed that intake of calcium should not fall below 400 mg per day. Insofar as level of calcium intake is implicated in growth it should be such that unequivocal stunting is prevented. The desirability of maximal rate and extent of growth also remains to be elucidated by further research.

2. It has been established beyond doubt that the development of rickets and dental caries is largely independent of calcium intake. The formerly high incidence in Europe and the United States of rickets in infants fed largely on cow's milk, and the fact that excellent teeth are often found in populations on low calcium diets, are examples that may be cited.

Adult life

Male. No frank signs of calcium deficiency have ever been described in any part of the world, even in populations with an habitually low calcium intake.

Female. In population groups with an habitually low calcium intake, repeated pregnancies and long lactations are common and have been associated, in certain limited regions, with the development of osteomalacia. This is clearly not due solely to the level of calcium intake. Thus in some parts of northern India, higher calcium intakes are found with frequent occurrence of osteomalacia; whereas in southern India, where there is a lower calcium intake, osteomalacia is rare (58). Moreover, the disease has not been reported in central and southern Africa. Apparently, if vitamin D status is satisfactory, osteomalacia with low calcium regimens

is not a problem. While it is generally recognized that this type of osteomalacia is due primarily to vitamin D deficiency, it cannot be ruled out that a low calcium intake is an exacerbating factor.

Old age

While much further work needs to be undertaken, limited evidence suggests that neither composition nor the physical density of bone are prejudiced by an habitually low intake of calcium. Senile osteoporosis, a very common disease of old age (64), is sometimes associated with a deficient absorption of calcium. It is thought by some investigators to be caused or favored by calcium deficiency (51, 69). Others are of the view that endocrine disorder is of major significance in this condition (1, 53). Unfortunately, the prevalence of the condition in populations with wide differences in calcium intake is not known.

SYSTEMIC EFFECTS

Serum calcium

While serum calcium is significantly lower (about 10 percent) in the population of some developing regions, it is not known to what extent the lower values are related to low intake (63). The effect of calcium enrichment of calcium-poor diets on the level of the element in the serum and its physiological significance require investigation. Elevation of the serum calcium level in such population groups has been accomplished by protracted feeding on a western diet, *inter alia*, high in calcium.

Breast milk

Several studies have shown the mean concentration of calcium to be normal in the breast milk of mothers used to a low calcium diet (21).

Present knowledge of the various physiological processes in man, directly or indirectly involving calcium, does not support the view that a low calcium intake is necessarily prejudicial to the normal performance of the body. On the other hand, the long-term studies of Sherman and his associates on rats cannot be disregarded, i.e., under the experimental conditions prevailing, a high calcium intake was beneficial in several respects, including reproduction and longevity (57).

HIGH INTAKES

The Group was not aware of any population studies showing deleterious effects resulting from an excessive calcium intake. There is, therefore, no information as to whether any problems would arise as a result of excessively high intakes in large population groups.

There are, however, some limited groups among whom the habitual intake of calcium is known to exceed 2 g to 3 g per day. These include ragi eaters in India (58), certain nomadic groups in east Africa and in Mauritania who consume almost exclusively milk diets, and large milk drinkers in western countries. There was no evidence before the Group that such high calcium intakes were detrimental to health, except probably in individuals with susceptibility to kidney stone formation (26, 41). Further information needs to be collected on the effects on health of habitually high intakes of calcium of 2 g and over per day.

4. CLINICAL AND THERAPEUTIC STUDIES WHICH MAY BE RELEVANT TO CALCIUM REQUIREMENTS

Certain pathological conditions do exist, most of them rare, however, in which an intake of calcium beyond the usual limits may be advisable. Further study of these conditions, which is greatly needed, may reveal that they are commoner than is presently believed. The following considerations are therefore included.

CONDITIONS IN WHICH CALCIUM DEFICIENCY MAY PLAY A PART

(*a*) osteopathy, which can occur in breast-fed premature infants having a birth weight of 800 g to 1200 g (54);

(*b*) various syndromes in children and adults in which grossly subnormal calcium absorption from the gut occurs, including many hereditary diseases (9), the large group of steatorrheas (44) and various forms of renal damage with and without hypercalciuria (10);

(*c*) senile osteoporosis, which is a very common condition of old age sometimes associated with a malabsorption of calcium (64), and which, limited evidence suggests to some investigators, may be associated with a deficient intake of calcium and may be cured by an intake of the order of 2.0 g a day (24).

CONDITIONS IN WHICH CALCIUM EXCESS MAY PLAY A PART

(*a*) idiopathic hypercalcemia of infancy (4, 13, 38, 55), in which normal intakes of calcium prove to be toxic and in which a reduction of intake to 100 mg a day or less, while the disease lasts, provides good therapy;

(*b*) sarcoidosis and hypothyroidism in which calcium overabsorption frequently occurs (29, 56);

(*c*) idiopathic hypercalciuria, presenting usually as chronic renal stone formation, in which calcium overabsorption frequently occurs and in which the hypercalciuria is exceedingly responsive to changes in calcium intake (26, 27).

In medical therapy of patients with skeletal disorders, tetany and so forth, dietary intakes of calcium of the order of 600 mg to 800 mg a day are adequate in support of the specific treatment being given.

Until more is known of the clinical syndromes resulting from an excess or deficiency of calcium intake in normal subjects or in those particularly sensitive subjects mentioned above, caution is needed where changes in the level of calcium intake are contemplated.

5. CALCIUM METABOLISM

The process of dissolution and reformation of the skeleton goes on throughout life (45, 50). There is a dynamic equilibrium between the calcium in the blood plasma and in the skeleton. The homeostatic control of calcium in the plasma is mainly mediated by the parathyroid glands and vitamin D. Both these factors exercise a direct action on the bone tissue, presumably linked up with the oxidative metabolism of the active cells, while vitamin D also influences the plasma calcium level by its action on the absorption of calcium from the intestinal tract.

The growing and the adult body have certain maintenance requirements. In addition, the growing body requires extra calcium in proportion to the growth of the skeleton. The final skeletal size, that is, its volume and total content of calcium, is determined genetically but is influenced by nutrition and by physical activity. However, we can postulate that additional calcium over and above the actual requirement will not lead to significant further bone formation.

The absorption of calcium and the urinary calcium excretion are highly correlated in adulthood (34). In equilibrium, some adults excrete 3 to 4 times as much calcium in the urine as others, which means that they absorb 3 to 4 times as much calcium. The factors responsible for such a correlation remain unknown, nor is it known whether the regulation concerns primarily the kidneys or the gut.

The urinary calcium is, on an average, not greatly influenced by variations in the daily intake of calcium. Malm (40) observed in his long-term studies that a reduction in the daily intake from 900 mg to 450 mg was followed by a 32-mg average reduction in urinary calcium. The variability is considerable: in some persons the urinary calcium output may not decrease at all, whereas it may be nearly halved in others. Population groups having diets habitually low in calcium also show a low mean urinary excretion.

The absorption of calcium depends on several factors. Vitamin D is the primary regulator (49). In vitamin D deficiency, in spite of an adequate intake of calcium, the net absorption of calcium is reduced and the balance may become negative.

Another factor important in its bearing on calcium requirements is the power of adaptation (see Chapter 1) to low calcium intake. The physiological basis of this mechanism is not yet understood but its existence is clear (20, 25, 30, 40, 48, 67). In the course of a negative calcium balance, induced in children or in adults as a result either of a lowering of the calcium intake or of the ingestion of a substance which interferes with the absorption of calcium, the absorption increases, that is, the fecal calcium falls and after a time the negative balance changes to a positive one or to a state of calcium equilibrium. The adaptive mechanism acts independently of the plasma calcium concentration.

This power of adaptation plays an important part in populations living on habitually low calcium diets. Under such conditions adaptation apparently also involves reduction in the urinary excretion of calcium. However, direct information is lacking on the relationship between calcium intake and urinary calcium in populations adapted to a low intake. Such information would allow a comparison with the findings of Malm (40) and Knapp (34) on populations where calcium intake is high.

6. INTERRELATIONS BETWEEN DIETARY CALCIUM AND OTHER NUTRIENTS

Interactions between calcium and other dietary and physiologic factors have long been known. The primary duty of the Group was not to annotate the many experimental studies of this kind but to evaluate their significance in relation to calcium requirements in man.

FACTORS WHICH INFLUENCE CALCIUM ABSORPTION AND RETENTION

Vitamin D

It is clear that satisfactory calcium metabolism is dependent upon an adequate supply of vitamin D, whether from diet or exposure to ultraviolet radiation (49). Neither the definition of an "adequate" supply of this vitamin nor a discussion of its function is within the scope of this report, although it is recognized that the requirements of vitamin D and calcium may be mutually interdependent.

It is important to note, therefore, that in the discussion of the possible significance of the various factors which may influence calcium metabolism, the assumption is made that vitamin D is adequately supplied.

Calcium/phosphorus ratio

Numerous studies, particularly in vitamin D deficient animals, have shown the calcium/phosphorus ratio to be one of the determinants in assessing calcium requirements. The diets of man, especially those consisting largely of vegetable products, almost invariably contain much more phosphorus than calcium. Furthermore, there is convincing evidence, obtained with human subjects, which demonstrates that the addition of

a rather large amount of phosphate to the diet has almost no effect on calcium absorption (39). Hence, the Group felt that variations in the calcium/phosphorus ratio in habitual diets are of no practical significance in human nutrition.

Phytic acid

While numerous short-term experiments in man and in animals have demonstrated that the administration of phytic acid, or materials high in phytic acid, may adversely affect calcium absorption (23) there is abundant evidence that early adaptation to such diets soon occurs (31, 33, 67).

These findings have been demonstrated in populations consuming large amounts of whole grain or lightly milled cereals and other vegetable products, the phytic acid of which theoretically should precipitate all dietary calcium. In almost all such populations a habitually low calcium intake is the rule. Although exceedingly large amounts of phytic acid, which have been used therapeutically to inhibit calcium absorption, may effectively do so for a time (28), there is little reason to believe that calcium requirements are influenced by the amount of this acid commonly encountered in human diets.

Protein, oxalates, fatty acids, citric acid and lactose

Experimental studies in animals have shown that oxalates and, to a much lesser extent, saturated fatty acids in rather large amounts may interfere with calcium absorption; and that variations in the amounts of protein, lactose, citric and various other acids in the diet may influence calcium absorption. There appears to be no evidence from long-term studies to suggest that the usual amounts of these substances encountered in every-day diets require serious consideration in the estimates of normal calcium requirements (60, 61).

It can be concluded that variations in the concentration of many components in the diet may temporarily influence calcium absorption or retention. Adaptive mechanisms, whatever they may be, rapidly ameliorate or abolish these effects unless the amounts involved are excessive. It is unlikely, therefore, that calcium needs are influenced to any serious degree by the amounts of such substances ordinarily consumed.

EFFECTS OF CALCIUM ON OTHER NUTRIENTS

Enrichment of the rations of experimental or farm animals with large amounts of calcium salts has occasionally been observed to produce adverse effects (8, 59). Precipitation of deficiencies of manganese, zinc, iron and iodine in experimental and farm animals has been reported, which can be corrected by the addition of the relevant nutrient to the ration. No comparable data are available for man.

In view of the widespread incidence of hypochromic anemia in many parts of the world, the possible relationship of calcium intake to iron utilization deserves further study, particularly in regions where an increase in the calcium intake is planned. There is no reason to believe at the present time, however, that a high calcium intake is an important etiologic factor in such anemias in persons whose usual diet is rich in calcium.

Impaired utilization of protein, fat and total energy has also been reported in animals fed large amounts of calcium.

7. METHODS OF ESTIMATING CALCIUM REQUIREMENTS

About 99 percent of the calcium in the body is in the skeleton. Calcium metabolism may thus be expected to be influenced greatly by the growth of the skeleton, its mineral content and total mass. Unfortunately, knowledge about the calcium content of the body at birth is very scanty; nor is it known whether the few adult bodies analyzed were representative of the western population from which they came. There is no reliable information as to whether or not race, climate and environmental factors influence the skeletal mass, although it is reasonable to assume that, with adequate nutrition, skeletal configuration and size are largely dictated by genetics.

Available data allow the assumption that the body at birth contains about 25 g to 30 g of calcium and in adults of 50 kg to 70 kg body weight from 850 to 1,400 g (36, 50). In the newborn the skeleton is only partly mineralized and it is reasonable to accept that the body contains at that stage about 0.8 percent calcium as against 1.7 percent at maturity. Rates of skeletal growth and mineralization as they relate to total body growth have been estimated, but they cannot be accurately defined until representative data on body composition and body calcium for contrasting populations are available at all stages of growth (32, 36). If variations in the growth process are disregarded, the accretion of about 1,200 g of calcium, a figure which has been assumed for a well-nourished western population over the 20-year period from birth to adulthood, would require an average daily retention of 165 mg. This figure would represent a reasonable approximation to the average daily calcium accretion of children and adolescents.

To arrive at a value for the minimum requirement, additions must be made to allow for incomplete absorption[1] and losses in urine and through

[1] Reference is made to apparent absorption, which is the difference between the calcium ingested and the fecal calcium. The latter includes calcium of both dietary and endogenous origin.

the skin. Assessment of the magnitude of these losses must await the results of future work. There is evidence, of course, that calcium does not accrue at a uniform rate, since the growth rate varies with age and may occur in spurts.

Some shortcomings of the balance method, in which intake and output of calcium are measured, have already been pointed out and cumulative errors inherent in it usually lead to unrealistically high retention values (11).[2] Nevertheless, it has served as the method of choice and it will continue to do so until better techniques are devised. The method can serve the useful purpose of estimating the point of equilibrium, that is, the situation in which calcium intake equals calcium output in the adult male. The intake at this point was formerly assumed to represent the minimum calcium requirement of the adult male (42).

The method was thoroughly explored and served as a basis for deriving the recommended dietary allowances of calcium (18). Mitchell and Curzon (42), after careful examination of existing data, expressed calcium requirement in relation to body weight. They then established that the scatter of results was no less when the intake of calcium was related to other parameters, such as body surface or height.

Important contributions in recent years have cast some further doubt on the validity of the short-term balance method of estimation. Thus, the much lower estimates of calcium required by Peruvians on habitually low calcium intakes — as contrasted with those obtained in the United States — and the experimental observations on Norwegians have established clearly that the body's adaptive mechanisms can achieve calcium equilibrium on intakes considerably below those of the subjects on whom earlier requirements were estimated (25, 40). It can, therefore, no longer be denied that the requirement estimates derived by this method are influenced by the habitual calcium intake of the subject under study.

The Group wished to point out that current knowledge does not permit any definite view of the relative merits of maintaining calcium equilibrium with relatively high or relatively low intakes, as it may influence the health of a given population. The important point is that populations with

[2] As an example, if the calcium intake, as measured, was 600 mg and the calcium in the excreta was 500 mg, this would give a measured retention of 100 mg. Failure to eat all food analyzed, if in error by 2 %, means that actual intake was 588 mg. Failure to collect all excreta, if in error by 2 %, means that actual excreta contained 510 mg. Actual net retention was 78 mg rather than 100 mg. Expressed in percentage, a 2 % error in balance data has introduced an error of nearly 30 % above the true retention.

habitually low intakes achieve equilibrium at lower levels than has previously been supposed and that populations accustomed to relatively high intakes can achieve equilibrium at lower intakes.

Other techniques have been of use in studies of calcium metabolism. Radioactive calcium (Ca^{45}) has been used to derive estimates of endogenous fecal calcium in animals and a few such studies have been conducted in man. It is doubtful, however, whether this tracer will receive wide use in human studies because of its hazards. X-ray measurements of bone structure and bone density have also proved valuable in experimental studies. It is again doubtful, however, whether these methods in their present stage of development are sufficiently practicable for determining the calcium status of a population. Furthermore, quantitative bone density measurements can conveniently be made only on certain bones of the extremities.

Methods using inert markers have been used extensively for many years in digestibility studies with ruminants. Such methods can be used for calcium metabolism studies in animals that possess a simple digestive system, if extreme care is taken to ensure that the marker is thoroughly mixed and uniformly distributed in the food.

Growth studies have long served to estimate the nutrient needs for growth in man and animals. Application of this method to calcium studies in children deserves further exploration under properly controlled experimental conditions, particularly in population groups whose calcium intake is low. Finally, careful epidemiological studies in populations with widely different calcium intakes, utilizing appropriate clinical and laboratory techniques, should contribute to current knowledge of the calcium needs of man.

8. ESTIMATES OF MINIMAL CALCIUM REQUIREMENTS

THE MINIMAL CALCIUM REQUIREMENTS OF ADULT MALES

No clear-cut disease due to calcium deficiency has ever been described in the human male. Deficiency disease can be produced experimentally in animals, but it is not possible to apply figures derived from such experiments to human nutrition. In consequence, current estimates of the minimal human requirement rest on balance studies and other indirect methods. Balance studies have been most commonly used.

Although it is possible to design (in theory) the ideal experiment, it would be nearly impossible to carry it out in man. The Group was limited, therefore, to the reports so far available. Clearly, balance experiments conducted with high levels of calcium in the diet are of little use in determining minimum requirements. However, in two studies done in recent years, an approximation to the lower level of calcium in the diet has been reached: the Peruvian prison study of Hegsted *et al.* (25) and the Oslo prison study of Malm (40). The results of these studies were as follows:

Hegsted *et al.* estimated that in the ten adult men studied, five required less than 200 mg, four required 300 mg to 400 mg and one 600 mg per day. The last-mentioned received calcium injections prior to experiment; his urinary calcium output, however, was not significantly higher than that of the others — in fact, it was identical with that of another subject and slightly above that of a second subject.

In the Oslo study, the calcium requirement for maintenance was estimated as 337 mg to 398 mg in nine subjects, 410 mg to 492 mg in twelve, 544 mg to 617 mg in four and 890 mg in one.

Some support in favor of the view that the lower figures arrived at in the above studies are near to the minimal requirement can be derived from the 1939 study in Ceylon of Nicholls and Nimalasuriya (46), where

it was also noted that adult Sinhalese males appear to develop near to normal skeletons in spite of a low calcium intake in childhood.

It is likely that skeletal size will influence the minimal daily calcium requirement, although the data available are inadequate for purposes of deriving actual figures. It is also probable that physical activity will be an influence, insofar as it is likely that high physical activity will result in a heavier skeleton. However, no data are yet available along these lines.

It is known that sweat contains calcium and experiments on adult males under severe sweating conditions for several hours have shown the calcium loss to be considerable (43). Further studies are required to determine to what extent long-term calcium losses through sweating would influence the minimal calcium requirement.

THE MINIMAL CALCIUM REQUIREMENT OF ADULT FEMALES

The average weight of the female skeleton is lower than that of the male and presumably the calcium requirement may be proportionately reduced. However, no suitable data are available to differentiate between the requirements of the two sexes.

Pregnancy and lactation impose an extra need on the adult female in proportion to the number of children produced and breast fed. The amount of calcium given to the fetus is about 30 g, which can be partly compensated for by adaptation (36, 50). A six-month period of lactation, however, results in the secretion in the milk of up to 50 g of calcium. It is doubtful if adaptation can fully compensate for such a loss in any woman, even on a high calcium diet.

A clear-cut calcium deficiency disease has never been described in women. On the other hand, it cannot be denied that diets low in calcium can probably contribute to producing osteomalacia in women on diets also deficient in vitamin D.

THE MINIMAL CALCIUM REQUIREMENTS OF CHILDREN

It appears that no frank ill effects attributable to calcium deficiency have so far been reported in children receiving an habitually low calcium diet. The report of Nicholls and Nimalasuriya from Ceylon (46), although inadequate in some respects, indicates that children of 4 to 7 years of age

on a mean daily intake of 200 mg of calcium develop fairly well. A mean daily retention of 115 mg and a mean urinary excretion of 15 mg daily were observed. Studies carried out in India (35) have shown that children in the 9 to 11 age group living habitually on diets providing a calcium intake of about 350 mg daily, retain about 120 mg daily (the mean daily urinary excretion being approximately 50 mg).

Broad experience of South African Bantu children also supports the view that a calcium intake only a little above 200 mg in the diet is sufficient to prevent obvious calcium deficiency (65, 66).

THE MINIMAL CALCIUM REQUIREMENT OF OLD AGE

Some balance studies indicate that old people will retain calcium avidly over periods of some months when additional calcium is provided in the food, and such findings have been used to support the view that old age osteoporosis can, in part, be due to an inadequate supply of calcium before the observation period. Recent reported results indicate that osteoporosis is frequently a calcium deficiency disease (51, 69). However, the evidence supporting this view is not yet convincing. Reliable observations along these lines are expected to be made in the next few years and the question should then be reviewed again.

9. CALCIUM REQUIREMENTS AND CALCIUM METABOLISM OF ANIMALS

There is nearly as much ignorance about the calcium requirement of farm animals as there is about the requirements of man. Only in a few areas of the world has experimental evidence been obtained and have scientific groups examined existing data and formulated allowances. Such allowances are under periodic review, the situation reflecting the paucity of current knowledge. "Requirements" is perhaps an ill-chosen term in this connection, since the situations governing animal production are shaped by man's needs.

Experimental work with laboratory animals, as also the unique physiological processes evident in milk and egg production, furnish pointers that may be useful in the consideration of man's calcium requirements. For example, it has been amply established that the retention of calcium in rats depends upon their body stores (12, 47, 48). Further studies on rats (30) and dogs (20) demonstrate a high capacity of adaptation to low intakes of calcium, and many studies confirm that no ill effects arise from relatively high calcium intakes, provided the diet is properly balanced in other nutrients. There is evidence that animals adapted to low calcium intakes eventually reach adult skeletal development similar to that of animals given diets richer in calcium. From the extensive studies of Sherman (5,57) it is clear that the animal can attain a satisfactory plateau of skeletal mineralization within a wide range of calcium intakes. It should be noted that the dietary calcium concentration of 0.34 percent, with which the rats in Sherman's experiments attained the optimum nutritional plateau, is approximately one third that of rats' milk.

Any attempt to apply data from farm animals to man must be tempered with the knowledge that heavy milk or egg production places abnormal stresses upon the animal. For example, the dairy cow in one lactation may well produce 10 metric tons, and exceptional cows have been known to produce 20 tons of milk. Now, 10 metric tons of milk contain 12 kg

of calcium, which is twice the average calcium content of the cow. However, artificial as the comparisons may be, heavy milk production involves stresses which may relate to consideration of calcium metabolism in human beings. There is evidence that milk fever, a characteristic disease of the heavy-producing cow, can be alleviated by restricting calcium intake for a few weeks *pre-partum*. Such dietary treatment stimulates and enhances calcium mobilization mediated through the parathyroids (3). There is further support from tracer studies for this view. Short-term or single dose tracer studies have their limitations in that misinterpretation may result from lack of equilibrium of the tracer in body tissues or fluids.

It should be noted that the dairy cow depletes skeletal reserves of calcium during heavy lactation and replenishes stores during the later phase of the reproductive cycle. Whether or not a cycle of depletion and repletion of calcium stores in lactating women is a normal physiological phenomenon is not known.

There is evidence from experimental animals of the preferential role of cancellous or medullary bone in the processes of calcium mobilization. Under carefully controlled dietary treatments, bone density measurements of experimental animals will not reveal calcium depletion unless it exceeds about 20 percent. This degree of accuracy has little value as a measure of bone density and of the effect of calcium intake thereon in a heterogeneous human population.

Balance studies with livestock lead to cumulative errors, all tending in the direction of an exaggeratedly high assessment of calcium retention (11). Available data suggest that a similar situation prevails in short-term balance studies in man.

Finally, the rate of maturation of experimental or domestic animals places them in sharp contrast to man. As an illustration, the bovine matures in two years, contrasted with twenty years for man. Any consideration of calcium accretion rates in animals as compared with those in man must be tempered with this knowledge.

10. CALCIUM INTAKE IN RELATION TO RADIOSTRONTIUM

Among the great number of fission products produced by nuclear explosions strontium-90 is of particular concern because of its long physical half-life of 28 years. Being a beta-emitter, strontium-90 does not contribute significantly to the external irradiation of any part of the body. However, on being taken into the body, it becomes incorporated into bone because of its chemical similarity to the bone-forming element calcium.

In view of this chemical and metabolic similarity between calcium and strontium and particularly as both these elements have a common route through the food chain (Soil → Plant → Animal → Man), a discussion of calcium requirements should take into consideration the possibility of diminishing the uptake and retention of radiostrontium by increasing the intake of calcium.

The chemical similarities between strontium and calcium make the use of Sr^{90}/Ca ratio convenient for following the movement of Sr^{90} from the environment to human bones. However, the chemical behavior of strontium and calcium is not identical and their utilization, therefore, differs in biological processes such as assimilation and excretion.

The differential behavior of strontium and calcium is caused by several physiological factors of which the most important are probably: preferential absorption of calcium from the gastrointestinal tract; preferential urinary excretion of strontium; preferential transfer of calcium from the blood into milk; and preferential transfer of calcium across the placental barrier.

The differential behavior of calcium and strontium has been expressed as Strontium-Calcium Observed Ratio (OR) and defined as follows:

$$\text{OR}_{\text{sample/precursor}} = \frac{Sr^{90}/Ca \text{ of sample}}{Sr^{90}/Ca \text{ of precursor}}$$

The use of this ratio is illustrated by its application to the use of food, where

$$\text{OR bone/diet} = \frac{\text{Sr}^{90}/\text{Ca of bone}}{\text{Sr}^{90}/\text{Ca of diet}}$$

Studies in experimental animals with radiostrontium have shown that the OR, bone/diet is higher (*a*) in young animals and (*b*) with low calcium diets. Many investigators have shown that adding calcium to the diet decreases the OR, bone/diet (22, 52, 68).

From evidence available at present, therefore, a possible protective measure against absorption and excessive accumulation of radiostrontium in the human skeleton seems to be a liberal supply of calcium in the diet, particularly during the period when the rate of calcium absorption is high, and when the usual intake of calcium is low. It must be pointed out, however, that while addition of calcium to the diet may reduce the absorption of radiostrontium, any effect in diminishing radiostrontium already incorporated in bone is highly unlikely.

Since milk constitutes a major dietary source of calcium in many countries, it is necessary to mention some experiments in which the use of diets with the same amount of calcium provided by milk and nonmilk sources yielded contradictory results. Thus, Comar *et al.* have concluded from short-term studies on rats that the absorption of calcium and uptake of strontium were higher with diets in which the dietary calcium was provided by milk than when it was provided from sources other than milk (6). Similar results have been obtained by Lengemann *et al.* in man (37). However, in long-term studies on rats, Gran observed that there was no change in the absorption and retention of radiostrontium when the source of calcium was changed from milk to sources other than milk (22). On the basis of available knowledge of the physiology of calcium and its metabolism, it would be expected that no difference would be encountered in long-term experiments when the source of the dietary calcium is changed.

Much further long-term research needs to be undertaken to determine absorption and retention of radiostrontium when the diet is high in calcium. The Group was pleased to note that this subject is already under consideration by groups of experts convened specially to consider its various aspects (16).

11. RECOMMENDATIONS ON CALCIUM NEEDS

The Group defined the *minimum requirement* of calcium for an adult as the smallest amount of that nutrient which will maintain health and keep the body in calcium balance over a period of years when the diet is otherwise adequate and the vitamin D status of the body is satisfactory.

The Group was conscious of the fact that such evidence as was available was not sufficient to allow it to specify a figure for the minimum adult requirement. The Group was not so much concerned with stating precisely the requirement of an individual, but rather with formulating its recommendations for the requirements of population groups. The conclusions reached on the question of calcium requirements were limited not only by the lack of evidence concerning the amount of the minimum requirement, but also by the fact that disorders and diseases attributable primarily to deficiency of dietary calcium have not been observed or reported in large populations subsisting habitually on intakes varying from 300 mg to 400 mg calcium per day. Some recent long-term balance studies have indicated that adults can adapt themselves successfully to an intake of calcium varying between 400 mg and 500 mg per day and even less. Such a range is higher than those observed in some parts of the world where no ill-effects attributable to calcium deficiency have been described. These bare facts, already considered earlier in this report, are reiterated as a prelude to a discussion of the question of requirements.

Suggested practical allowance

In view of the difficulty of defining quantitatively the minimum calcium requirement, the Group thought that the use of the term " average minimum requirement " was not justified in this report. It decided to recommend a range, rather than attempt to cite a single figure, in order to avoid giving an impression of accuracy which was not considered to be warranted in

the present limited state of knowledge. The recommendations with regard to calcium allowances are, therefore, based on different considerations from those which underlie the recommendations of the Committee on Protein Requirements (15). For these reasons, definition of such terms as " average requirement " and " optimal requirement " has not been attempted, although this was done by the Committee on Protein Requirements. The Group adopted instead the term " suggested practical allowance."

Suggested practical allowance is defined, for the purpose of this report, as the intake at which the needs of the great majority of persons in any defined population group are likely to be adequately met. It can, therefore, be considered a safe allowance. The possibility of undesirable effects on the health of a population with an average calcium intake habitually below this level should be borne in mind. Although knowledge gained from animal experiments may suggest the nature of such adverse effects, the symptoms and the possibility of their onset in man below any given level of calcium intake cannot be predicted with certainty.

Adults

In view of the scanty available evidence, a single figure for the lowest practical allowance could not reasonably be proposed. In the Group's opinion, intakes between 400 mg and 500 mg per day would represent the suggested practical allowance for adults. Since a lower intake of calcium is habitual in some large groups of populations in which no ill-effects attributable to calcium have been described, the Group was unable to conclude that the usefulness of raising an intake above the suggested practical allowance has been definitely proved.

The average intake of calcium in several countries is known to be considerably higher than 500 mg a day. Average intakes between 800 mg and 1,000 mg a day are found in some countries and of 1,000 mg to 1,500 mg a day in some population groups. The Group found no evidence that a daily intake as high as 1,500 mg was undesirable. It, therefore, did not suggest alteration in the calcium intake of large groups of people whose dietary habits provide such a level. The Group, however, was of the view that raising the calcium intake beyond one gram was unlikely to serve any physiologically useful purpose.

The scarcity of available information (see Chapter 3) did not allow the Group to make any suggestions about the upper limit of calcium

intake beyond which signs and symptoms of toxicity would supervene. In this respect, individuals with special susceptibility, such as those liable to kidney stone formation, may require special consideration.

Children and adolescents

Recommendations of allowances for nutrients during the growing period from infancy through adolescence have to take into account the needs not only for maintenance but also for continued accretion of calcium for purposes of skeletal growth. Unfortunately, a great deal of uncertainty exists about the rate of skeletal growth in children. The rate of growth, as judged by changes either in weight or in height, is not constant during the whole growth period. Weight and height increase rapidly during the first year of life. During the succeeding eight to ten years, prior to puberty, weight increase is relatively slow and gain in height is relatively greater than that in weight during this period. Also, the percentage of calcium in the body is greatly augmented (from approximately 0.8 percent at birth to approximately 1.7 percent in adulthood) during the growth period.

Many calculations of the expected annual increment in calcium required to produce the adult skeleton have been made (32), the most recent being that of Leitch and Aitken (36). In the latter, the authors assume the increment in calcium to be proportional to the increase in weight and also that the proportional increase of calcium in the body parallels the gain in body weight. Such calculations postulate the need for a high intake of calcium to provide for the growth spurt at puberty. On the other hand, increase in height follows a pattern quite distinct from that of weight and it may be equally logical to relate calcium needs to changes in height. The Group, in view of these considerations and aware of the evidence of reasonable growth in children on relatively low calcium diets, felt that the division of the growth period into several age groups would be unwise. Moreover, for reasons discussed earlier, it was decided to recommend a range of suggested practical allowances, instead of a minimum requirement, as follows:

Age	*Suggested practical allowances (mg per day)*
0 to 12 months (not breast fed)	500 to 600
1-9 years	400 to 500
10-15 years	600 to 700
16-19 years	500 to 600

It has been assumed that the adequately breast-fed infant receives sufficient calcium for its needs. The amounts recommended for artificially fed infants are based on the lower of those values found in the current feeding practices of western countries. The Group realized that children and adolescents may have an intake of calcium higher than that indicated above, even reaching a level of 1,500 mg per day, depending upon age, food habits and other factors. In the opinion of the Group the available evidence does not indicate that such a high intake is undesirable, as already stated in an earlier section (p. 11). No suggestion was made, therefore, for any alteration in the current dietary practice involving such intakes.

Sex

The Group was of the opinion that there was no evidence for recommending different allowances for boys and girls, or for adult males and nonpregnant and nonlactating women.

Pregnancy and lactation

The growth of the fetus, particularly during the last trimester of pregnancy, may require about 30 g of calcium. Additional drain on the maternal organism occurs during lactation. The daily output of breast milk has been assumed as 850 cc, as in the earlier reports of the Committees on Calorie and Protein Requirements. On this basis, approximately 300 mg of calcium a day will be needed by the body. Given a lactation period of six months, the additional calcium need may amount to about 50 g, and this would increase if lactation continued for a longer period. The total additional calcium requirement in pregnancy and lactation together would thus be between 80 g and 100 g or even more, depending upon the amount of milk produced. Taking into consideration also the possibly more efficient utilization of dietary calcium during lactation, the Group concluded that the suggested practical allowance should be between 1,000 mg and 1,200 mg per day. An intake within these limits should be provided during the third trimester of pregnancy and throughout the period of lactation. The Group realized, however, that in certain populations, successful repeated pregnancies and lactations are achieved with a calcium intake much below the suggested allowance. Extensive observations to determine if any demonstrable ill effects on the health of the mothers occur under such conditions are obviously needed.

Old age

Certain recent work suggests that an inadequacy of dietary calcium may be one of the causes of senile osteoporosis, a condition which has been found to be fairly common in some countries in individuals over 60. However, the available evidence was not considered sufficient to permit the assessment of any special allowance for this age group. This question should be reviewed after the results of further research become available.

Physical activity

The Group did not recommend additional intake of calcium with respect to physical activity because of the lack of relevant evidence that such is needed.

12. RECOMMENDATIONS FOR FUTURE RESEARCH

It is readily apparent from the preceding chapters of this report that definitive information upon which calcium requirements can be based is extremely limited. As indicated in the Introduction, the Group considered it useful to emphasize the inadequacy of the data available in the hope that appropriate research may be stimulated as soon as possible. Direct human studies should be the most useful; in particular, the "natural experiments" provided by large population groups consuming different amounts of calcium should be adequately utilized. However, much of the information required can be obtained only with experimental animals, and such studies should be encouraged. The Group wishes to call special attention to the desirability of encouraging studies on the various subhuman primates, since their nutritional requirements may be more analogous to those of man than to the requirements of some of the other laboratory animals in common use.

Composition of the human body with special reference to calcium

Information is needed on the total calcium content and the proportion of calcium and other constituents in the human body. Data should be collected on different population groups with regard to age, race and diets differing in calcium content.

Studies on bone

1. Basic studies on the histology, biochemistry and physics of bone and the influence of age and diet should be encouraged.
2. The Group particularly recommends that co-operative efforts be made for the collection and thorough examination of bones from all age groups in different regions of the world. Particular attention should be given to those bones which are known to have a high rate of calcium turnover, such as the vertebrae.

FOOD CONSUMPTION AND COMPOSITION WITH SPECIAL REFERENCE TO CALCIUM

1. The assessment and formulation of nutrition programs requires knowledge of the level and patterns of food consumption.

2. Accurate information is required on the composition of food *as eaten.* Inasmuch as there are interrelations between calcium and other nutrients, the analysis should not be limited to calcium alone. It should be noted that the introduction of new strains and of new agricultural practices may change the composition of foods. Thus food analysis should be a continuous effort.

3. Particular attention should be paid to unusual sources of calcium both in dietary surveys and in studies on food composition. These include the water supply and certain methods of food processing, as well as those foods which have a naturally high calcium content.

4. The Group was not impressed with the likelihood that the nature of the diet will markedly affect calcium requirements. Nevertheless, studies on the availability of calcium in foods should be encouraged. In this regard, it would be useful to formulate a standard reference diet to provide a common base line of comparison for studies in different laboratories.

DETERMINATION OF MINIMUM CALCIUM REQUIREMENTS

1. Long-term balance studies, in which the calcium intake should be deliberately varied, need to be done both on children and adults with different nutritional backgrounds.

2. Investigations on the methodology used in balance studies would be useful. Particular attention should be paid to the assessment of the magnitude of the errors in such studies; and the possibility of improving and simplifying procedures, for example by the use of fecal markers, deserves attention.

3. Adequately designed growth and balance studies should be undertaken on children. Populations living on low calcium diets are the most appropriate experimental subjects and differences in calcium intake should be the sole variable insofar as this can be achieved.

4. The effects of repeated pregnancies and long lactations should be determined in the women of different population groups in relation to the varying levels of calcium in their customary diets.
5. The influence of physical activity on calcium balance and calcium requirements requires investigation.

Determination of the maximum tolerated dietary levels of calcium

The difficulties of defining minimal needs are also encountered in defining maximum tolerated levels of calcium. In view of the large amounts consumed by some individuals and population groups, additional studies on both man and experimental animals should be undertaken in this field. Particular attention should be given to the possible importance of inter-relationships between the intake of calcium and that of other dietary constituents.

Population studies

Attention has already been drawn to the necessity of extensive study of those population groups habitually consuming very high or very low levels of calcium. The Group wishes to re-emphasize the importance of such studies utilizing modern metabolic, clinical and histologic methods.

Physiology and biochemistry of calcium metabolism

An adequate appreciation of the role of dietary calcium in health and disease requires a thorough understanding of calcium metabolism. The Group recommended that additional efforts be made in the following areas:

1. study of the factors and mechanisms involved in the absorption of calcium and its re-excretion;
2. definition of the magnitude of endogenous calcium excretion under various conditions;
3. determination of the relationships between calcium intake and the level of calcium in the plasma and other plasma constituents which may influence this relationship; this is particularly important in view of the evidence that certain populations on habitually small intakes of calcium have lower levels in the plasma;

4. study of the magnitude and factors controlling dermal losses of calcium;
5. investigation of mechanisms and factors controlling the "adaptive" process;
6. continuing study of the interrelations between dietary calcium and other elements, particularly with regard to iron, magnesium and the trace elements.

Disorders and diseases involving calcium

Those conditions in which calcium metabolism is known or suspected to be abnormal require extensive study utilizing all the appropriate epidemiological, clinical, histologic and biochemical methods. Such studies are justified in their own right and may contribute significantly to knowledge of normal calcium metabolism. Attention is called specifically to the need for study of:

1. the role of calcium intake in the etiology and treatment of senile osteoporosis;
2. calcium intake in relation to renal stone formation;
3. other clinical conditions which may result from an excess or deficiency of dietary calcium;
4. the etiology of those diseases which involve soft tissue calcification;
5. specific pathologic conditions in which an intake beyond the recommended limits may be advisable.

Tests of calcium deficiency

Increased efforts should be made in the search for methods of detecting calcium deficiency or for the evaluation of nutritional status with regard to calcium. Improved radiologic techniques offer some promise, and methods for the biochemical evaluation of calcium in the blood, tissues and excreta should be improvised.

Influence of dietary calcium on radiostrontium retention

Further long-term research is needed to determine the role of dietary calcium in the absorption and retention of radiostrontium under varying dietary conditions and at different ages.

PRIORITIES IN RESEARCH

The results which will be obtained from specific research proposals can seldom be predicted with certainty. Nevertheless, there are some areas of research particularly relevant to the establishment of calcium requirements which appear more likely to yield significant practical results in the near future than others. The Group wished to reiterate those which, in its opinion, fall into this category and thus deserve emphasis, though the items listed are not in order of priority:

(*a*) basic studies on the histology, biochemistry and physics of bone in relation to age and growth;

(*b*) the collection and examination of bones from different regions, especially those bones, such as the vertebrae, which have a high rate of calcium turnover;

(*c*) the relationship between calcium intake and calcium balance and growth;

(*d*) thorough study of population groups habitually consuming very high or very low levels of calcium;

(*e*) the relationship between calcium intake and level of calcium in the plasma and other plasma constituents, such as proteins, which may be influential;

(*f*) the effects of different levels of calcium intake on health in repeated pregnancy and lactation;

(*g*) the role of dietary calcium in the etiology and treatment of osteoporosis.

CALCIUM IN THE FOOD SUPPLIES OF SELECTED COUNTRIES BASED ON FAO FOOD BALANCE SHEETS

Country and year	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruit	Meat and poultry	Eggs	Fish	Milk and products	Total supply of Ca
EUROPE										
Denmark (1957/58)										
mg Ca/cap/day	61	25	13	94	17	16	9	16	749	1 000
Percentage of total Ca supply	6	3	1	9	2	2	1	2	74	100
Finland (1958/59)										
mg Ca/cap/day	70	19	3	30	11	7	9	10	1 170	1 329
Percentage of total Ca supply	5	1	—	2	1	1	1	1	88	100
France (1958/59)										
mg Ca/cap/day	46	19	13	178	18	17	13	8	618	930
Percentage of total Ca supply	5	2	1	19	2	2	1	1	67	100
Italy (1958/59)										
mg Ca/cap/day	59	9	24	190	26	6	10	5	381	710
Percentage of total Ca supply	8	1	3	27	4	1	1	1	54	100
Norway (1958/59)										
mg Ca/cap/day	52	20	9	50	23	8	9	22	833	1 026
Percentage of total Ca supply	5	2	1	5	2	1	1	2	81	100
NORTH AMERICA										
Canada (1957/58)										
mg Ca/cap/day	34	13	12	64	24	17	21	6	856	1 047
Percentage of total Ca supply	3	1	1	6	2	2	2	1	82	100

CALCIUM IN THE FOOD SUPPLIES OF SELECTED COUNTRIES BASED ON FAO FOOD BALANCE SHEETS (*continued*)

Country and year	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruit	Meat and poultry	Eggs	Fish	Milk and products	Total supply of Ca
United States (1958)										
mg Ca/cap/day	29	10	18	135	21	18	24	5	856	1 116
Percentage of total Ca supply	3	1	2	12	2	2	2	—	76	100
LATIN AMERICA										
Argentina (1957)										
mg Ca/cap/day	45	28	5	44	27	29	11	2	460	651
Percentage of total Ca supply	7	4	1	7	4	5	2	—	70	100
Chile (1957)										
mg Ca/cap/day	45	19	34	108	11	6	5	12	280	520
Percentage of total Ca supply	9	4	7	20	2	1	1	2	54	100
NEAR EAST AND AFRICA										
Israel (1957/58)										
mg Ca/cap/day	80	8	37	172	53	6	23	9	496	884
Percentage of total Ca supply	9	1	4	19	6	1	3	1	56	100
South Africa (1958)										
mg Ca/cap/day	53	3	10	54	19	11	4	8	280	442
Percentage of total Ca supply	12	1	2	12	4	2	1	2	64	100
Turkey (1957/58)										
mg Ca/cap/day	125	8	35	108	30	4	2	1	234	547
Percentage of total Ca supply	23	1	6	20	6	1	—	—	43	100

CALCIUM IN THE FOOD SUPPLIES OF SELECTED COUNTRIES BASED ON FAO FOOD BALANCE SHEETS (*concluded*)

Country and year	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruits	Meat and poultry	Eggs	Fish	Milk and products	Total supply of Ca
United Arab Republic (1957/58)										
mg Ca/cap/day	87	3	31	140	35	4	2	5	142	449
Percentage of total Ca supply	19	1	7	31	8	1	—	1	32	100
ASIA AND FAR EAST										
India (1957/58)										
mg Ca/cap/day	98	6	67	23	5	—	—	1	147	347
Percentage of total Ca supply	28	2	19	7	1	—	—	—	43	100
Japan (1958)										
mg Ca/cap/day	66	22	91	101	5	1	5	19	58	368
Percentage of total Ca supply	18	6	25	28	1	—	1	5	16	100
OCEANIA										
Australia (1958/59)										
mg Ca/cap/day	39	11	10	85	37	26	1	4	620	833
Percentage of total Ca supply	5	1	1	10	4	3	—	1	75	100
New Zealand (1958)										
mg Ca/cap/day	40	13	11	98	29	23	19	6	926	1 165
Percentage of total Ca supply	3	1	1	8	3	2	2	1	79	100

CALCIUM INTAKES OF SELECTED GROUPS OF PEOPLE IN DIFFERENT COUNTRIES BASED ON DIETARY SURVEYS

Country	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruit	Meat and poultry	Eggs	Fish	Milk and products	Total Ca	Unit surveyed
EUROPE											
United Kingdom[1]	*Note*: 243 mg of creta praeparata added to the cereals.										
mg Ca/cap/day	290	25	—	46	16	23	19	14	591	1 024	Country wide
Percentage of total Ca supply	28	2	—	4	2	2	2	1	58	99	
NORTH AMERICA											
United States[2]											
Urban											
mg Ca/cap/day	167	11	16	81	37	37	24	incl. in	716	[3]1 111	6 000 households
Percentage of total Ca supply	15	1	2	7	3	3	2	meat	64	99	
Rural nonfarm											
mg Ca/cap/day	212	12	24	74	32	34	26	"	722	[3]1 160	"
Percentage of total Ca supply	18	1	2	6	3	3	2	"	62	99	"
Rural farm											
mg Ca/cap/day	222	14	25	79	30	33	32	"	855	[3]1 320	"
Percentage of total Ca supply	17	1	2	6	2	3	2	"	65	100	"

SOURCES: [1] *Strontium*-90 *in human diet in the United Kingdom 1958* - Agric. Research Council Radiobiological Laboratory Report No. 1, H.M.S.O., London, 1959

[2] *Dietary levels of households in the U.S.* - Household Food Consumption Surveys 1955, Report No. 6, U.S. Department of Agriculture, Washington, D.C.

[3] Miscellaneous foodstuffs included in total calcium figure.

CALCIUM INTAKES OF SELECTED GROUPS OF PEOPLE IN DIFFERENT COUNTRIES BASED ON DIETARY SURVEYS (*continued*)

Country	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruit	Meat and poultry	Eggs	Fish	Milk and products	Total Ca	Unit surveyed
LATIN AMERICA											
Venezuela[4]							and milk prods.				
mg Ca/cap/day	59	12	71	37	12	17	172	—	433	[3] 865	769
Percentage of total Ca supply	7	1	8	4	1	2	20	—	50	99	persons
NEAR EAST AND AFRICA											
Ivory Coast[5] Village											
mg Ca/cap/day	3	271	14	12	3	14	—	419	—	736	
Percentage of total Ca supply	—	37	2	2	—	2	—	57	—	100	7 254 persons
Encampment mg Ca/cap/day	1	336	2	28	7	27	—	389	—	790	
Percentage of total Ca supply	—	43	—	4	1	3	—	49	—	100	

[3] Miscellaneous foodstuffs included in total calcium figure.

[4] GONZALEZ S., Una encuesta alimentaria en las familias *Arch. Venez. de Nutrición*, Vol. VII, No. 2, p. 167, 1956.

[5] Territoire de la Côte-d'Ivoire. *Enquête de nutrition-Niveau de Vie, subdivision de Bongouanou*, 1955-56.

CALCIUM INTAKES OF SELECTED GROUPS OF PEOPLE IN DIFFERENT COUNTRIES BASED ON DIETARY SURVEYS (*concluded*)

Country	Cereals	Starchy roots	Pulses and nuts	Vegetables	Fruit	Meat and poultry	Eggs	Fish	Milk and products	Total Ca	Unit surveyed
Ethiopia[6]											Out of 6 200 people, 1 300 gave dietary information
mg Ca/cap/day	495	2	32	73	—	4	—	—	—	[9] 640	
Percentage of total Ca supply	77	5	5	11	—	1	—	—	—	99	
ASIA AND FAR EAST											
India[7]											
mg Ca/cap/day	128	—	76	80	2	—	5	—	160	[9] 469	83 692 persons
Percentage of total Ca supply	27	—	16	17	—	—	1	—	34	99	
Japan[8]											
mg Ca/cap/day	53	9	101	64	9	1	8	55	34	[9] 384	Nation-wide
Percentage of total Ca supply	14	2	26	17	2	—	2	14	9	99	

[6] *Ethiopia Nutrition Survey*. A Report by I.C.N.N.D. (U.S.A.), 1959.

[7] Indian Council of Medical Research, Special Report Series No. 25. *A supplement to the Results of Diet Surveys in India* 1935-48 by K. Mitra, New Delhi, 1953.

[8] Ministry of Health and Welfare, Japan. *Nutrition in Japan*, 1958.

[9] Miscellaneous foodstuffs included in total calcium figure.

Appendix 3

CALCIUM INTAKES OF GROUPS OF PEOPLE ACCORDING TO AGE AND SEX IN SELECTED COUNTRIES BASED ON INDIVIDUAL DIETARY SURVEYS

Country and group	Average dietary calcium intake (mg per caput per day)	
	Male	*Female*
British Solomon Islands[1] (Typical diet of a bush family)		
Adult male	777	
Adult female		541
Adolescents	541	
Children		
2-5 years old	270	
5-9 " "	505	
Colombia (Barranquilla)[2] (Diet of a typical working class family)		
Adult male	1 443	
Adult female		870
Children		
Male 16 years old	950	
Female 9 " "		1 034
Male 3 " "	826	
Other members of the household	950	857
Jamaica (rural areas)[3]		
Children and adolescents		
7-8 years old	290	
9-10 " "	280	
11-12 " "	300	260
13-14 " "	290	
13-17 " "		260
15-19 " "	440	

SOURCES: [1] South Pacific Health Service, 1952. *A survey of nutrition in the British Solomon Islands Protectorate*, by S. Holmes.

[2] La Alimentación de la Clase Obrera en Barranquilla. *Anales de economía y estadística*, Colombia, March 1952.

[3] MACKAY, I.F.S., STAFFORD, D., WILSON, K. and FOX, H.C. Dietary Survey of Jamaican Children. *J. Amer. Diet. Assoc., 34,* 603, 1958.

CALCIUM INTAKES OF GROUPS OF PEOPLE ACCORDING TO AGE AND SEX IN SELECTED COUNTRIES BASED ON INDIVIDUAL DIETARY SURVEYS (*concluded*)

Country and group	Average dietary calcium intake (mg per caput per day)			
Netherlands[4]	Higher social class		Lower social class	
	1951	1952	1951	1952
Children 7-9 years old				
Male	1 130	1 150	840	880
Female	1 110	1 050	860	790
All groups	1 120	1 090	850	840

New Guinea[5]	Biak		Sorong	
3-6 years old	300		420	
6-10 " "	286		340	
10-15 " "	375		196	
18-50 " "	*Male* 440	*Female* 359	*Male* 282	*Female* 201

Nigeria[6]	Kanuri and Shuwa farmers and cattlemen	Otukwang Clan farmers	Camberri farmers	Ibo and Yoruba clerks
Children				
4-6 years old	1 100	300	300	
10-12 " "		400	400	500

United States[7]	Western region		North-Central Region		Northeastern Region			
			Iowa	Five other states	Pennsylvania		Rhode Island	
	Male	Female	Female		Male	Female	Male	Female
5-12 years old	[8] 1 200	[8] 1 060						
13-15 " "	1 390	950						
16-17 " "	1 440	980			1 515	979		
18-19 " "					1 482	921		
20-29 " "					1 241	901		
30-39 " "	[8] 1 190	[8] 780	560	560 - 890				
40-49 " "			510	200 - 620				
50-59 " "	860	600	460	360 - 530				
60-69 " "	880	630	490	360 - 550				
70-79 " "	790	650	430	260 - 640			419-	504-
80 and over	880	460					1 177	1 039

SOURCES: [4] Abstract of a Report of the Dutch Nutrition Council on the Nutrition Survey 1951/52 published by *Voeding*, 16, No. 7, 1955, pp. 636-646.

[5] Malcom, S. H. *A study of food intake in two areas in New Guinea*, South Pacific Commission, Noumea, New Caledonia, April 1958.

[6] Nicol, B. M. The Nutrition of Nigerian Children with particular reference to their Energy Requirements. *British J. of Nutrition*, vol. 10, No. 3, 1956, p. 181.

[7] (a) *Co-operative nutritional status studies in the western region. I. Nutrient Intake.* Western Regional Research Publication No. 383.

(b) *Food intakes of 2,189 women in five north-central states.* North Central Region Publication No. 83.

(c) FISHER, K. H. and DODDS, M. L. Calcium intake of adolescents and young adults. *J. Amer. Diet. Assoc. 34*, 392, 1958.

(d) TUCKER, R. E., BRINE, C. L. and WALLACE, M. S. Nutrition intake of older institutionalised persons. *J. Amer. Diet. Assoc. 34*, 819, 1958.

[8] Utah only.

APPLICATION OF THE RECOMMENDATIONS

(Note by the Secretariats of FAO and WHO)

This Note was prepared independently of the Group after the final text of the report was completed. It is intended to illustrate the application of the Group's findings to the estimation of the calcium requirements of relatively large population groups. For this purpose the distribution of the population in three hypothetical countries is shown in the Annex at the end of the note. Average *per caput* requirement is calculated by multiplying the percentage of the population within each age group by the suggested practical allowance for that age group and dividing the aggregate figure by 100. Thus, in Country A for example, the *per caput* practical allowance would be in the range 440 mg to 540 mg of calcium per day.

It will be seen that populations containing more young persons would have higher *per caput* allowances. It is also apparent, however, from comparing the results for Countries A, B and C that rather large differences in population distribution will have relatively little effect on the average *per caput* allowances. This, of course, would not hold true when more limited groups — orphanages, educational institutions, etc. — are concerned.

The suggested practical allowance for the last trimester of pregnancy and the whole period of lactation was established as 1,000 mg to 1,200 mg. The FAO Committee on Calorie Requirements recommended that the number of pregnancies could be assumed to be 10 percent more than the number of infants between 0 and 1 year of age (14). Thus, in Country A the number of pregnant women would be equivalent to 3.6 percent of the population and in Country C to 1.7 percent. However, since an additional calcium allowance is made only during the last trimester of pregnancy, there would be only the equivalent of 1.2 and 0.6 percent, respectively, to be taken into account. Even if the practical allowances are considered at the higher values in the range suggested, no significant effect on the needs of the population will be caused by failure to make a specific adjustment for this group.

It will be noted that the practical allowance for the artificially fed infant is 500 mg to 600 mg; for the adult woman, 400 mg to 500 mg; and for the lactating woman, 1,000 mg to 1,200 mg. Thus the total need of an adult female and an artificially fed baby is essentially the same as that of a lactating woman. It is most convenient, therefore, to utilize the system shown in the table and consider all infants as artificially fed and all women as nonlactating in calculating the needs of a country or a large population group.

Finally, in the application of the recommendations of the Committees on Calorie Requirements and Protein Requirements it was assumed that approximately 10 percent of the available calories and protein would be lost as waste (14, 15). However, the recommendations of the Group considering calcium needs provide a range of values, e.g., 400 mg to 500 mg per day for adults. By using the higher value, there would appear to be a sufficient margin for losses by waste with no additional allowance required.

It should be stressed again (see Chapter 2) that food balance sheets are of limited value with regard to calcium and that wastage of calcium may be higher than that of some other nutrients. This is borne out by the fact that the parts of foodstuffs often discarded in commercial or home preparation (milling of cereals, peeling of vegetables, discarding of leaves, etc.) may be those most rich in calcium. Emphasis should also be placed on the need for estimates of the calcium content of water supplies and on the possible addition of calcium salts in the preparation of foods.

PER CAPUT DAILY PRACTICAL ALLOWANCES OF CALCIUM FOR THREE HYPOTHETICAL COUNTRIES

Age group	Suggested practical allowance	Country A		Country B		Country C	
		Population distribution	Calcium required	Population distribution	Calcium required	Population distribution	Calcium required
years	mg	%	mg	%	mg	%	mg
0-1	500-600	3.3	1 650- 1 980	1.9	950- 1 140	1.5	750- 900
1-9	400-500	21.8	8 720-10 900	15.6	6 240- 7 800	14.1	5 640- 7 050
10-15	600-700	14.1	8 460- 9 870	10.8	6 480- 7 560	7.7	4 620- 5 390
16-19	500-600	8.2	4 100- 4 920	6.9	3 450- 4 140	5.0	2 500- 3 000
19 +	400-500	52.6	21 040-26 300	64.8	25 920-32 400	71.7	28 680-35 850
Total		100	43 970-53 970	100	43 040-53 040	100	42 190-52 190
Average per caput practical allowance of calcium in mg per day			440-540	—	430-530	—	420-520

Appendix 5

LIST OF PARTICIPANTS

MEMBERS

Professor C. E. DENT	Department of Medicine, University College Hospital Medical School, London, England
Professor R. W. ENGEL	Head, Department of Biochemistry and Nutrition, Virginia Polytechnic Institute, Blacksburg, Va., U.S.A.
Dr. D. M. HEGSTED	Associate Professor, Department of Nutrition, Harvard University School of Public Health, Boston, Mass., U.S.A.
Dr. S. K. KON	Head, Department of Nutrition, National Institute for Research in Dairying, Shinfield, Reading, England
Dr. A. NELSON	Chief, Division of Medicine, Research Institute of National Defence, Sundbyberg, Sweden
Professor R. NICOLAYSEN	Director, Institute for Nutrition Research, University of Oslo, Blindern, Norway
Dr. P. Royer	Professeur agrégé à la Faculté de Médecine, Paris, France
Dr. H. K. STIEBELING	Director, Institute of Home Economics, Agricultural Research Service, U.S. Department of Agriculture, Washington, D.C., U.S.A.

Dr. M. SWAMINATHAN	Head, Division of Dietetics, Central Food Technological Research Institute, Mysore, India
Dr. R. TARJAN	Director, Nutrition Institute, Budapest, Hungary
Dr. A.R.P. WALKER	Human Biochemistry Research Unit, South African Institute for Medical Research, Johannesburg, South Africa
Professor F. G. YOUNG (Chairman)	Department of Biochemistry, University of Cambridge, England

FAO

Dr. M. AUTRET	Director, Nutrition Division
Dr. H. D. CREMER	Chief, Applied Nutrition Branch, Nutrition Division
Dr. K.K.P.N. RAO	Chief, Food Consumption and Planning Branch, Nutrition Division

WHO

Dr. V. N. PATWARDHAN	Research Officer, Nutrition Unit
Dr. S. K. REDDY	Nutrition Unit

BIBLIOGRAPHY

1. ALBRIGHT, F. & REIFENSTEIN, E. C., JR. *The parathyroid glands and metabolic bone disease.* Baltimore, Williams and Wilkins, 1948.
2. AYKROYD, W. R. & KRISHNAN, R. S. B. G., *Lancet*, 235:153, 1938.
3. BODA, J. M., *J. Dairy Sci.*, 39:66, 1956; 37:360, 1954.
4. BONHAM CARTER, R., DENT, C. E., FOWLER, D. & HARPER, C. M., *Arch. Dis. Childh.*, 30:399, 1955.
5. CAMPBELL, H. L. & SHERMAN, H. C., *Amer. J. Physiol.*, 144:717, 1945.
6. COMAR, C. L., WASSERMAN, R. H. & NOLD, M. M., *Proc. Soc. exp. Biol. Med.*, 92: 859, 1956.
7. CRAVIOTTO, R. O., ANDERSON, R. K., LOCKHART, E. E., MIRANDA, F. P. & HARRIS, R. S., *Science*, 102:91, 1945.
8. DAVIS, G. K., *Fed. Proc.*, 18:1119, 1959.
9. DENT, C. E. & HARRIS, H., *J. Bone Joint Surg.*, 38B:204, 1956.
10. DENT, C. E., HARPER, C. M. & PHILPOT, G. R., *Quart. J. Med.*, 30:1, 1961.
11. DUNCAN, D. L., *Nutr. Abstr. Rev.*, 28:695, 1958.
12. FAIRBANKS, B. W. & MITCHELL, H. H., *J. Nutr.*, 11:551, 1936.
13. FANCONI, G., GIRARDET, P., SCHLESINGER, B., BUTLER, N. & BLACK, J., *Helv. paediat. Acta*, 7:314, 1952.
14. FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS. *Calorie requirements.* Rome. FAO Nutritional Studies No. 15, 1957.
15. FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS. *Protein requirements.* Rome. FAO Nutritional Studies No. 16, 1957.
16. FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS. *Radioactive materials in food and agriculture.* Rome. FAO Atomic Energy Series No. 2, 1960.
17. FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS. *Handbook for the preparation of food balance sheets.* Washington, D. C., 1949.
18. FOOD AND NUTRITION BOARD, NATIONAL RESEARCH COUNCIL. *Recommended dietary allowances.* Washington, D.C. Publication No. 589, 1958.
19. FOURMAN, P. *Calcium metabolism and the bone.* Oxford, Blackwell, 1960.
20. GERSHOFF, S. N., LEGG, M. A. & HEGSTED, D. M., *J. Nutr.*, 64:303, 1958.
21. GOPALAN, C. & BELAVADY, B. Proceedings of the fifth international congress on nutrition, *Fed. Proc.*, 20, Suppl. 7:177, 1961.
22. GRAN, F. C., *Acta physiol. scand.*, 48, Suppl. 167, 1960.

23. HARRIS, R. S., *Nutr. Rev.*, 13:257, 1955.
24. HARRISON, M., FRASER, R. & MULLAN, B., *Lancet*, 1:1015, 1961.
25. HEGSTED, D. M., MOSCOSO, I. & COLLAZOS, C., *J. Nutr.*, 46:181, 1952.
26. HENNEMAN, P. H., *Fed. Proc.*, 18:1093, 1959.
27. HENNEMAN, P. H., BENEDICT, P. H., FORBES, A. P. & DUDLEY, H. R., *New Engl. J. Med.*, 259:802, 1958.
28. HENNEMAN, P. H., CARROLL, E. L. & ALBRIGHT, F., *Ann. N.Y. Acad. Sci.*, 64:343, 1956.
29. HENNEMAN, P. H., DEMPSEY, E. F., CARROLL, E. L. & ALBRIGHT, F., *J. clin. Invest.*, 35:1229, 1956.
30. HENRY, K. M. & KON, S. K., *Brit. J. Nutr.*, 7:147, 1953.
31. HOFF-JØRGENSEN, E., ANDERSEN, O. & NIELSEN, G., *Biochem. J.*, 40:555, 1946.
32. HOLMES, J. O., *Nutr. Abstr. Rev.*, 14:597, 1945.
33. IRVING, J. T. *Calcium metabolism.* New York, Wiley, 1957.
34. KNAPP, E. L., *J. clin. Invest.*, 26:182, 1947.
35. KURIEN, P. P., NARAYANARAO, D., SWAMINATHAN, M. & SUBRAMANYAN, V., *Brit. J. Nutr.*, 14:339, 1960.
36. LEITCH, I. & AITKEN, F. C., *Nutr. Abstr. Rev.*, 29:314, 1959.
37. LENGEMANN, F. W., COMAR, C. L. & WASSERMAN, R. H., *J. Nutr.*, 61:571, 1957.
38. LIGHTWOOD, R., *Arch. Dis. Childh.*, 27:302, 1952.
39. MALM, O. J., *Scand. J. clin. Lab. Invest.*, 5:75, 1953.
40. MALM, O. J., *Scand. J. clin. Lab. Invest.*, 10, Suppl. 36, 1958.
41. MELICK, R. A. & HENNEMAN, P. H., *New Engl. J. Med.*, 259:307, 1958.
42. MITCHELL, H. H. & CURZON, E. G. *The dietary requirement of calcium and its significance.* Paris, Herman. Actualités scientifiques et industrielles No. 771, 1939.
43. MITCHELL, H. H., HAMILTON, T. S. & HAINES, W. T., *J. biol. Chem.*, 178:345, 1949.
44. NASSIM, J. R., SAVILLE, P. D., COOK, P. B. & MULLIGAN, L., *Quart. J. Med.*, 28: 141, 1959.
45. NEUMAN, W. F. & NEUMAN, M. W. *The chemical dynamics of bone mineral.* Chicago, University of Chicago Press, 1958.
46. NICHOLLS, L. N. & NIMALASURIYA, A., *J. Nutr.*, 18:563, 1939.
47. NICOLAYSEN, R., *Acta physiol. scand.*, 5:200, 1943.
48. NICOLAYSEN, R., *Acta physiol. scand.*, 36:114, 1956.
49. NICOLAYSEN, R. & EEG-LARSEN, N., *Vitamins and Hormones*, 11:29, 1953.
50. NICOLAYSEN, R., EEG-LARSEN, N. & MALM, O. J., *Physiol. Rev.*, 33:424, 1953.
51. NORDIN, B.E.C., In *Bone as a tissue*, ed. by K. Rodahl, J. T. Nicholson & E. M. Brown, pp. 46-66, New York, McGraw-Hill, 1960.
52. PALMER, R. F., THOMPSON, R. C. & KORNBERG, H. A., *Science*, 127:1505, 1958.
53. REIFENSTEIN, E. C., In *Bone as a tissue*, ed. by K. Rodahl, J. T. Nicholson & E. M. Brown. New York, McGraw-Hill, 1960.
54. ROSSIER, A., PAUPE, J., MICHELIN, J. & LARNAUDIE, L., *Arch. franç. Pédiat.*, 15:477, 1958.

55. ROYER, P. & FREDERICH, A., *Actualités néphrologiques de l'Hôpital Necker*, 1:55, 1960, Paris, Flammarion.

56. ROYER, P., LESTRADET, H. & HABIB, R., *Arch. franç. Pédiat.*, 15:896, 1958.

57. SHERMAN, H. C. *Calcium and phosphorus in foods and nutrition.* New York, Columbia University Press, 1947.

58. SUBRAHMANYAN, V., NARAYANARAO, M., RAMARAO, G. & SWAMINATHAN, M., *Brit. J. Nutr.*, 9:350, 1955.

59. Symposium on interaction of mineral elements in nutrition and metabolism. DAVIS, G. K., Chairman. *Fed. Proc.*, 19:635, 1960.

60. TARJÁN, R., SÁNDI, E. & DÉNES, A., *Acta physiol. Acad. Sci. hung.*, 5, 313: 1954.

61. TARJÁN, R., SÁNDI, E. & DÉNES, A., *Acta physiol. Acad. Sci. hung.*, 5:463, 1954.

62. TECHNICAL COMMISSION OF THE HEALTH COMMITTEE, LEAGUE OF NATIONS. Report on the physiological basis of nutrition. *Quart. Bull. Hlth Org. L. o. N.*, 5, 1936.

63. TROWELL, H. C. *Non-infective disease in Africa.* London, Arnold, 1960.

64. URIST, M. R., In *Bone as a tissue*, ed. by K. Rodahl, J. T. Nicholson & E. M. Brown, pp. 18-45, New York, McGraw-Hill, 1960.

65. WALKER, A.R.P., *Ann. N. Y. Acad. Sci.*, 69:989, 1958.

66. WALKER, A.R.P., Proceedings of the fifth international congress on nutrition, *Fed. Proc.*, 20, Suppl. 7:328, 1961.

67. WALKER, A.R.P., FOX, F. W. & IRVING, J. T., *Biochem. J.*, 42:452, 1948.

68. WASSERMAN, R. H., COMAR, C. L. & PAPADOPOULOU, D., *Science*, 126:1180, 1957.

69. WHEDON, G. D., *Fed. Proc.*, 18:1112, 1959.